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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/721,114	11/22/2000	Hirohiko Hirochika	MAFF-1	2997

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EXAMINER	
BAUM, STUART F	

ART UNIT	PAPER NUMBER
1638	

DATE MAILED: 06/30/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/721,114	HIROCHIKA ET AL.	
	Examiner	Art Unit	
	Stuart F. Baum	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 April 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 12-16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 12-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *22 November 2000* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

RCE Acknowledgment

1. The request filed on 4/9/2004 for a Request for Continued Examination (RCE) under 37 C.F.R. § 1.114, based on parent Application No. 09/721,114 is acceptable and a RCE has been established. An action on the RCE follows.

Claims 1 and 12-16 are pending.

Claims 12-16 have been newly added.

2. Claims 1 and 12-16 are examined in the present office action.

Claim Objections

3. Claim 12 is objected to for being dependent on a canceled claim. For purposes of compact prosecution, claim 13 will be examined as if it is dependent on claim 1. Correction is requested.

Specification

4. Objection is made to the specification for not incorporating SEQ ID NO's when referring to nucleic acid or amino acid sequences. 37 CFR 1.821(d) requires the use of the assigned sequence identifier (e.g. SEQ I.D. NO: X) in all instances where the description or claims of a patent application discuss sequences. See page 10, line 33 and page 11, line 1, for example.

Objection is made to the specification for not including a complete reference citation when referencing a document. See page 9, lines 27-29.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

5. Claims 1 and 12-16 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a substantial asserted utility or a well established utility.

Applicants claims are drawn to an isolated polynucleotide encoding a plant polypeptide involved in brassinosteroid signal transduction comprising amino acids 1 to 1057 of SEQ ID NO:2 or an amino acid sequence with at least 80% homology to SEQ ID NO:2, wherein a plant which has a defect in said polynucleotide exhibits dwarfism, upright form and malformation of grain hulls or said plant is brassinosteroid insensitive, or wherein said polynucleotide comprises the nucleic acid sequence from position 655 to position 3825 of SEQ ID NO:1.

Applicants report the isolation of a genomic DNA from rice by transposon tagging/plasmid rescue. Applicants purport that said genomic DNA when mutant because of the insertion of a Tos17 transposon is responsible for a dwarf rice phenotype. The isolated genomic DNA from the plasmid rescue was used as a probe to isolate a cDNA clone from a cDNA library (pages 9-12, Examples 1-5). The sequence of the cDNA clone is set forth as SEQ ID NO:1 encoding SEQ ID NO:2. Applicants disclose that the normal function of the protein encoded by SEQ ID NO:1 is lost because of the insertion of the Tos17 transposon, which creates a longer mRNA molecule compared to a plant not containing the Tos17 transposon (pages 11-12, Example 4).

Applicants have disclosed that their invention relates to a novel gene in plants which encodes a protein having the function of controlling an in-vivo signal transduction system in a

physiological reaction system against brassinosteroid hormone (page 1, 1st paragraph). Applicants disclose that their invention relates to methods for controlling various effects in plant in which brassinosteroid hormone is involved, e.g., growth promotion, yield increase, quality improvement, maturation enhancement and tolerance against biotic and abiotic stresses (paragraph bridging pages 3 and 4). However, based upon Applicant's disclosure, there is no clear nexus between their invention of SEQ ID NO:1 and any utility set forth to allow one skilled in the art at the time the invention was made to take the claimed invention and clearly and immediately achieve the benefits set forth.

The state-of-the-art teaches to properly ascertain that a mutant gene is responsible for a particular phenotype, the mutant plant must be complemented with a wild-type allele of the suspected gene. Walbot (1992, Annu. Rev. Plant Physiol. Plant Mol. Biol. 43:49-82) teaches "proof of function requires recovery of a wild-type allele and demonstration of complementation of the mutant defect" (page 70, last paragraph). Therefore, given that Applicants teach that a regenerated rice plant can contain anywhere from 5 to 30 copies of the Tos17 retrotransposon (page 3 1st paragraph), it is not clear if the dwarfed phenotype is due to a disruption of the endogenous cloned sequence by the Tos17 retrotransposon or if another copy of the Tos17 retrotransposon is disrupting another gene. Given the high number of retrotransponsons in a regenerated rice plant, more than one gene can contain a copy of the Tos17 retrotransposon. Without a complementation analysis, one skilled in the art would not know for certain the identity of the gene which is responsible for the dwarf rice phenotype.

In regards to Applicant's SEQ ID NO:1, how and under what conditions should a nucleic acid encoding SEQ ID NO:2 be used to control growth promotion, yield increase, quality

improvement, maturation enhancement, or tolerance against biotic and abiotic stresses? Does one skilled in the art want to increase the activity of the encoded polypeptide of SEQ ID NO:2 or decrease its activity in a plant, and in what organ, tissues or cell types? It is apparent that extensive further research, not considered to be routine experimentation, would be required before one skilled in the art would know how to use the claimed invention. It has been established in the courts that a utility which requires or constitutes carrying out further research to identify or reasonably confirm a "real world" context of use is not a substantial utility:

> "The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. Unless and until a process is refined and developed to this point—where specific benefit exists in currently available form—there is insufficient justification for permitting an application to engross what may prove to be a broad field." (*Brenner v. Manson,* 383 U.S. 519 (1966)).

Thus, while a developmental process such as growth promotion or quality improvement would provide substantial benefit to the public, it is unclear how one of ordinary skill in the art would be able to utilize Applicant's nucleic acid of SEQ ID NO:1 encoding SEQ ID NO:2 to control any physiological processes without having to carry out further research to verify that the claimed sequence actually is involved in the claimed growth processes . Accordingly, the claimed invention lacks a "real-world" use.

In addressing claims drawn to sequences having 80% homology to SEQ ID NO:2, since SEQ ID NO:1 encoding SEQ ID NO:2 lacks utility for the reasons set forth above, sequences having less than 100% sequence identity to SEQ ID NO:2 would also lack utility. Again, Applicant should note that no region of the protein encoded by SEQ ID NO:2 has been identified to be essential for its proper acitivy. Also, no working examples of any such sequence having 80% homology to SEQ ID NO:2 are set forth in Applicant's disclosure.

Additionally, there also is no well-established utility for SEQ ID NO:1 encoding SEQ ID NO:2. SEQ ID NO:1 does not have a well-established utility for hybridization purposes because the encoded protein does not have utility for the reasons indicated above. Accordingly, the claimed invention lacks utility.

Applicants' Remarks

Applicant's arguments filed 4/9/2004 have been fully considered but they are not persuasive.

Applicants disagree with the Examiner's statement that the creation of dwarf plants is not an asserted utility in the specification. Applicants contend that the specification asserts that the polynucleotides of the invention can be used to control growth, e.g., to create dwarf plants (page 5, middle paragraph).

The Office contends that this remark is moot based on the present office action.

Applicants contend that the specification discloses that plants lacking the claimed polynucleotide exhibit dwarfism, upright form, and malformation of grain hulls and that they are brassinosteroid insensitive and that plants genetically engineered to have a defect in said polynucleotide would exhibit these phenotypes (page 5, last paragraph). Applicants contend that reliable methods to inhibit the expression of genes in plants including co-suppression and antisense were part of the state-of-the-art at the time of filing (page 6, top paragraph).

The Office contends that Applicants have not demonstrated that the claimed polynucleotide is responsible for the specified phenotypes as discussed above. Assuming that Applicants cloned sequence is responsible for the specified phenotypes, methods of gene silencing produce unpredictable results. For example, Colliver et al (1997, Plant Mol. Biol.

35:509-522) showed that tranformation of bird's foot trefoil with a construct that was antisense to bean chalcone synthase unexpectedly resulted in transformants with *increased* levels of chalcone synthase transcripts (page 519, left column, 2nd paragraph). Montgomery et al (Trends in Genetics, July 1998, 14(7):255-258) teach that not all transgenes can cause co-suppression in plants and that there is no basis for predicting which transgenes would have this effect (page 257, column 1, last paragraph). Emery et al (2003, Current Biology 13:1768-1774) disclose experiments in which a target sequence of a micro-RNA was changed by two base-pairs. The altered base-pairs caused the complementary micro-RNA not to bind to the target sequence, which subsequently led to an increased expression of the target sequence's encoded protein (page 1769, right column, 2nd full paragraph).

Applicants contend that the demonstration that plants lacking the claimed polynucleotides exhibit these phenotypes obviates the Examiner's citation of Altmann.

The Office contends that this remark is moot based on the present office action.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1 and 12-16 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Applicants' Remarks

Applicant's arguments filed 4/9/2004 have been fully considered but they are not persuasive.

Applicants contend that the polynucleotides of the present invention can be used to produce a plant that has a defect in said polynucleotide and that such a plant would exhibit dwarfism, upright form, and malformation of grain hulls and/or brassinosteroid insensitive. Applicants also contends that antisense and co-suppression are known in the art and are predictable (page 7, last paragraph).

The Office contends that Applicants have not demonstrated that the cloned sequence when mutant, is responsible for the specified phenotype, as discussed above and antisense and co-suppression produce unpredictable results, as discussed above.

Written Description

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1, 12 and 14-15 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants claims are drawn to an isolated polynucleotide encoding a plant polypeptide involved in brassinosteroid signal transduction comprising an amino acid sequence with at least 80% homology to SEQ ID NO:2.

Applicants isolated their invention from rice by transposon tagging/plasmid rescue of a gene that Applicants purport is responsible for a dwarf phenotype. The isolated DNA from the plasmid rescue was used as a probe to isolate a cDNA clone from a cDNA library (pages 9-12, Examples 1-5). The sequence of the clone is set forth as SEQ ID NO:1 encoding SEQ ID NO:2.

The Applicants do not identify essential regions of the protein encoded by SEQ ID NO:1, nor do Applicants describe any polynucleotide sequences that encode a polypeptide with at least 80% homology to SEQ ID NO:2 that encodes a functional protein of SEQ ID NO:2. It is noted that Applicants do not disclose a specific activity for the claimed sequence. The Federal Circuit has recently clarified the application of the written description requirement to inventions in the field of biotechnology. See University of California v. Eli Lilly and Co., 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). In summary, the court stated that a written description of an invention requires a precise definition, one that defines the structural features of the chemical genus that distinguishes it from other chemical structures. A definition by function does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. The court goes on to say, "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus." *See University of California v. Eli Lilly and Co.*, 119 F.3d 1559; 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

Applicants fail to describe a representative number of polynucleotide sequences encoding a protein with the same activity as the polypeptide of SEQ ID NO:2 falling within the scope of the claimed genus of polynucleotides that encode a polypeptide with at least 80% homology to SEQ ID NO:2. Applicants only describe a single cDNA sequence of SEQ ID NO:1. Furthermore, Applicants fail to describe structural features common to members of the claimed genus of polynucleotides. Hence, Applicants fail to meet either prong of the two-prong test set forth by *Eli Lilly*. Furthermore, given the lack of description of the necessary elements essential for the protein of SEQ ID NO:2, it remains unclear what features identify a rice protein of SEQ ID NO:2. Since the genus of proteins having the same activity as the protein of SEQ ID NO:2 has not been described by specific structural features, the specification fails to provide an adequate written description to support the breath of the claims.

Enablement

8. Claims 1 and 12-16 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claimed invention is not supported by an enabling disclosure taking into account the *Wands* factors. *In re Wands,* 858/F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988). *In re Wands* lists a number of factors for determining whether or not undue experimentation would be required by one skilled in the art to make and/or use the invention. These factors are: the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or

absence of working examples of the invention, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breadth of the claim.

Applicants claims are drawn to an isolated polynucleotide encoding a plant polypeptide involved in brassinosteroid signal transduction comprising amino acids 1 to 1057 of SEQ ID NO:2 or an amino acid sequence with at least 80% homology to SEQ ID NO:2, wherein a plant which has a defect in said polynucleotide exhibits dwarfism, upright form and malformation of grain hulls or said plant is brassinosteroid insensitive.

Applicants report the isolation of a genomic DNA from rice by transposon tagging/plasmid rescue. Applicants purport that said genomic DNA when mutant because of the insertion of a Tos17 transposon is responsible for a dwarf rice phenotype. The isolated genomic DNA from the plasmid rescue was used as a probe to isolate a cDNA clone from a cDNA library (pages 9-12, Examples 1-5). The sequence of the cDNA clone is set forth as SEQ ID NO:1 encoding SEQ ID NO:2. Applicants disclose that the normal function of the protein encoded by SEQ ID NO:1 is lost because of the insertion of the Tos17 transposon, which creates a longer mRNA molecule compared to a plant not containing the Tos17 transposon (pages 11-12, Example 4).

Applicants have not taught by way of disclosure or example how to use the claimed sequence to produce an agronomically useful plant. Applicants report that their invention relates to brassinosteroid signal transduction but Noguchi et al (1999, Plant Physiology 121:743-752) teach that "there is little known about how brassinosteroid biosynthesis and signaling are coordinated. Brassinosteroids are synthesized using sterols as precursors, but much less is

understood about how sterols are funneled into brassinosteroid biosynthesis" (page 744, left column, bottom paragraph). Given the lack understanding about brassinosteroid signaling, one skilled in the art would not know how to use Applicants' sequence without much undue trail and error experimentation.

Applicants have not disclosed how one makes or isolates any of the sequences that are encompassed by Applicants' broad claims. Applicants have not taught which regions of SEQ ID NO:1 can be used to amplify any of said polynucleotides or which regions can be used as a probe to isolate any of said polynucleotide sequences.

The state-of-the-art is such that one of skill in the art cannot predict which polynucleotides encoding a polypeptide with at least 80% homology to SEQ ID NO:2 will encode a protein with the same activity as a protein whose amino acid sequence is set forth in SEQ ID NO:2. The prediction of protein structure from sequence data and, in turn, utilizing predicted structural determinations to ascertain functional aspects of the protein, is extremely complex, and the positions within the protein's sequence where amino acid substitutions can be made with a reasonable expectation of maintaining function are limited (Bowie et al, Science 247:1306-1310, 1990, see especially page 1306). Proteins may be sensitive to alterations in even a single amino acid in a sequence. For example, the replacement of a glycine residue located within the START domain of either the PHABULOSA or PHAVOLUTA protein receptor with either an alanine or aspartic acid residue, alters the sterol/lipid binding domain (7, see especially page 710, left column, 2nd paragraph).

In the absence of guidance, undue trial and error experimentation would be required for one of ordinary skill in the art to screen through the multitude of non-exemplified sequences

from any plant, either by using non-disclosed fragments of SEQ ID NO:1 as probes or by designing primers to undisclosed regions of SEQ ID NO:2 and then one skilled in the art would have to mutagenize the endogenous nucleic acid sequence in vivo which includes, mutagenizing a population of seeds, growing up the seeds, collecting the M1 seeds, planting the M1 seeds and screening for plants exhibiting a dwarf phenotype, screening through the dwarf plants for those in which the said sequence is mutagenized and then complement the mutant with an isolated sequence that was isolated using the above methods, in order to identify those, if any, that when mutant cause a dwarf phenotype, malformed grain hulls and are brassinosteroid insensitive and exhibit 80% homology with SEQ ID NO:2.

Therefore, given the breadth of the claims; the lack of guidance and examples; the unpredictability in the art; and the state-of-the-art as discussed above, undue experimentation would be required to practice the claimed invention, and therefore the invention is not enabled.

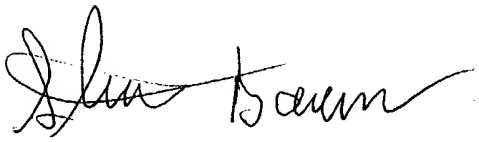
9. Claims 1, 12-16 are deemed free of the prior art, given the failure of the prior art to teach or reasonably suggest an isolated polynucleotide of SEQ ID NO:1 encoding SEQ ID NO:2.

10. No claims are allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stuart F. Baum whose telephone number is 571-272-0792. The examiner can normally be reached on M-F 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on 571-272-0804. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.



Stuart F. Baum Ph.D.
Patent Examiner
Art Unit 1638
June 24, 2004